e) enumerating any individual differentiated epithelial cancer cells found in situ in the free volume in the container;
f) examining the cell morphology of any individual differentiated epithelial cancer cells *in situ* in the free volume in the container;
g) said combining steps being performed either before or after the blood sample is placed in the container; and
h) said enumerating and examining steps being performed in no particular order.

2.(twice amended) A method for detecting the presence or absence of cancerous cell morphology in individual circulating epithelial cells in a centrifuged sample of anticoagulated whole blood contained in a container which container also contains an insert which forms a free volume in the container, said blood sample having been combined with one or more labeling agents that are specific to one or more epitopes on the epithelial cells, and said blood sample having also been combined with a colorant which is operable to clarify epithelial cell morphology in individual epithelial cells in the blood sample, said method comprising the steps of identifying a percentage of all individual labeled epithelial cells which are disposed in said free volume in situ in the container, and examining the cell morphology of any such individual identified epithelial cells *in situ* in the container so as to determine whether any such individual identified epithelial cells display cancerous cell morphology.

3.(twice amended) A method for identifying individual circulating cancerous epithelial cells in a centrifuged sample of anticoagulated whole blood which sample is contained in [an at least partially] a transparent container, which container also contains an insert, and which blood sample has been combined with at least one labeling agent that is specific to at least one epithelial cell epitope, and which blood sample has also been combined with a colorant that clarifies nucleated cell morphology, said method comprising the steps of examining a free volume located between the insert and the container wall wherein buffy coat constituents in the blood sample gravitate during centrifugation and enumerating any individual labeled epithelial cells having cancerous morphology *in situ* in the container, which individual labeled epithelial cells have localized during centrifugation in said free volume in the container.

4.(twice amended) A method for differentiating individual cancer cells from individual hematologic progenitor cells and from other nucleated cells in a sample of anticoagulated whole blood, said method comprising the steps of:

a) providing a sample of anticoagulated whole blood containing epitopic cell labeling materials which are operable to differentiate cancer cells and hematologic progenitor cells from each other and from other nucleated cells in the sample, said sample being contained in [an at least partially] a transparent container which also contains an insert that is operable to form a well-defined free volume in the container;

b) centrifuging the sample of blood in the container so as to gravimetrically separate the blood sample into its formed constituent components and so as to cause any nucleated cells which are not conventional blood cells in the sample to localize in said well-defined free volume in the container; and

c) examining said well-defined free volume in the container in order to determine whether any cancer or hematologic progenitor cells are present in said well-defined free volume in the container.

C' cont.

5.(twice amended) A method for detecting individual cancer cells and/or individual hematologic progenitor cells in a sample of anticoagulated whole blood, said method comprising the steps of:

a) providing a sample of anticoagulated whole blood containing cell epitope labeling materials which are operable to differentiate cancer cells and/or hematologic progenitor cells from other nucleated cells in the sample, said sample being contained in [an at least partially] a transparent container which also contains an insert that is operable to form a well-defined free volume in the container;

b) centrifuging the sample of blood in the container so as to gravimetrically separate the blood sample into its constituent formed components and so as to localize any nucleated cells in the sample in said well-defined free volume in the container;

c) examining said well-defined free volume in the container in order to determine whether any epitopically differentiated nucleated cells are present in said well-defined free volume in the container; and

d) enumerating any individual cancer cells and/or individual hematologic progenitor cells which are found to be present in said well-defined free volume in the container.

6.(twice amended) A method for analyzing a sample of anticoagulated whole blood in order to determine the presence or absence of individual cancer cells in the sample, said method comprising the steps of:

a) providing a sample of anticoagulated whole blood containing cell epitope-labeling materials which are operable to differentiate cancer cells from other nucleated cells in the sample, said sample being contained in [an at least partially] a transparent container which also contains an insert that is operable to form a well-defined free volume in the container;

b) centrifuging the sample of blood in the container so as to gravimetrically separate the blood sample into its constituent formed components and so as to deposit [any] individual cancer cells in the sample, in said well-defined free volume in the container; and

c) examining said well-defined free volume in the container in order to determine whether any individual differentiated cancer cells are present in said well-defined free volume in the container.

C' cont.

7.(twice amended) A method of identifying individual circulating epithelial cancer cells in a centrifuged sample of anticoagulated whole blood which sample is contained in [an at least partially] a transparent container, which container also contains an insert that forms a well defined free volume in the container, and which blood sample has been combined with at least one labeling agent that is specific to at least one epithelial cancer cell epitope, said method comprising the steps of examining said well-defined free volume in the container wherein white cells and platelets in the blood sample have gravitated during centrifugation and identifying any individual labeled epithelial cancer cells *in situ* in the container which labeled cells have localized in said well-defined free volume in the container during centrifugation of the sample in the container.

8. 9.(twice amended) A method for detecting the presence or absence of individual circulating nucleated epithelial cells in an anticoagulated whole blood sample, said method comprising the steps of:

C2

a) providing [an at least partially] a transparent container having a bore containing an

insert, said container and insert combining to form a well-defined free volume in the container bore;

b) combining the blood sample with one or more epitope-specific labeling agents so as to differentially highlight [any] individual nucleated epithelial cells which may be present in the blood sample;

c) combining the blood sample with a colorant which is operable to clarify cell morphology in [all] individual nucleated cells in the blood sample;

C2 cont'd

d) placing the blood sample in the container and centrifuging the blood sample in the container so as to cause [any] individual nucleated epithelial cells present in the blood sample to gather in said well-defined free volume in the container bore;

e) enumerating [any] individual labeled epithelial cells found in situ in the well-defined free volume in the container bore;

f) examining the cell morphology of any individual labeled cells *in situ* in the well-defined free volume in the container;

g) said combining steps being performed either before or after the blood sample is placed in the container; and

h) said enumerating and examining steps being performed in no particular order.

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17 ~~18~~.(twice amended) A method for detecting the presence or absence of individual circulating [hematopoietic] hematologic progenitor nucleated cells in an anticoagulated whole blood sample, said method comprising the steps of:

a) providing [an at least partially] a transparent container having a bore which contains an insert, said container and insert combining to form a well-defined free volume between said insert and a wall of said container bore which well-defined free volume has a transverse thickness that is at least about ten microns;

C3

b) combining the blood sample with one or more labeling agents which are specific to surface receptors on ~~hematopoietic~~ hematologic progenitor cells so as to differentiate any individual [hematopoietic] hematologic progenitor cells from other formed components in the blood sample;

c) combining the blood sample with a colorant which is operable to clarify cell morphology in all nucleated cells in the blood sample;

d) placing the blood sample in the container and centrifuging the blood sample in the container so as to cause [any] individual [hematopoietic] hematologic progenitor cells

present in the blood sample to gather in said well-defined free volume in the container;
e) examining the well-defined free volume under magnification and enumerating [any] individual differentiated [hematopoietic] hematologic progenitor cells found in situ in the well-defined free volume in the container;
f) examining under magnification the cell morphology of [any] individual differentiated cells *in situ* in the well-defined free volume in the container;
g) said combining steps being performed either before or after the blood sample is placed in the container; and
h) said enumerating and examining steps being performed in no particular order.

C3 Cancel.

13
~~14~~.(twice amended) A method for detecting the presence or absence of individual circulating cancer cells in a centrifuged sample of anticoagulated whole blood contained in a container which container also contains an insert that forms a well-defined free volume in the container, said blood sample having been combined with one or more epitope-specific labeling agents that are operative to produce a characteristic signal result on individual cancer cells, [which result can include no signal at all,] and which result is defined by the presence [or absence] of one or more epitopes on the individual cancer cells, and said blood sample having also been combined with a colorant which is operable to clarify cell morphology in all nucleated cells in the blood sample, said method comprising the steps of identifying by cell morphology all nucleated cells disposed in said well-defined annular free volume, and further characterizing all identified individual nucleated cells as cancer cells or non-cancer cells epitopically, said identifying and characterizing steps being performed *in situ* in the container.

REMARKS

Claim 14 stands rejected under 35 USC §112, second paragraph, as being indefinite due to the inclusion of the phrase "which result can include no signal at all".

Claims 3-7, 9 and 13 stand rejected under 35 USC §112, first paragraph, as being unsupported by the specification as originally filed due to the inclusion of the phrase "an at least partially transparent container". We believe that the Examiner meant also to include Claim 1 in this rejected claim group, since it includes the same phrase.